=> d his

L6

(FILE 'HOME' ENTERED AT 12:52:19 ON 27 NOV 2002)

115 INTRA(2A)NASAL?

FILE 'CAPLUS' ENTERED AT 12:52:27 ON 27 NOV 2002 11 S APOMORPHIN? AND (IMPOTEN? OR ERECTIL? (3A) DYSFUNCT?) AND (INTR Ll 37 S EL-RASHIDY, ?/AU L2 L30 S L1 AND L2 L413 S L2 AND APOMORPHINE L5 8 S L4 AND ERECT? => s 14 and (intranasal? or nasal? or intra(2a)nasal?) 4527 INTRANASAL? 13241 NASAL? 38151 INTRA 13241 NASAL?

0 L4 AND (INTRANASAL? OR NASAL? OR INTRA(2A)NASAL?)

=> s apomorphin? and (impoten? or erectil?(3a)dysfunct?) and (intranasal? or nasal? or intra(2a)nasal?)

9406 APOMORPHIN?

1640 IMPOTEN?

1242 ERECTIL?

32428 DYSFUNCT?

911 ERECTIL? (3A) DYSFUNCT?

4527 INTRANASAL?

13241 NASAL?

38151 INTRA

13241 NASAL?

115 INTRA (2A) NASAL?

L1 11 APOMORPHIN? AND (IMPOTEN? OR ERECTIL?(3A)DYSFUNCT?) AND (INTRANA SAL? OR NASAL? OR INTRA(2A)NASAL?)

=> d l1 abs ibib kwic 1-11

AB

L1 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2002 ACS

Erectile dysfunction (ED) (impotence) is a widespread, age-related problem, which affects 52% of men between 40 and 70 yr of age. It is classified as psychogenic, org., or mixed psychogenic and org. ED is not a problem only of men, because the relationship between partners can also be disturbed. Therefore, adequate treatment of ED is needed and the most convenient and simplest way is oral drug therapy. Sildenafil, phosphodiesterase-(PDE)-5-selective inhibitor has been the drug of choice for patients with ED since it has been launched in Mar. 1998. The results of various studies have confirmed the efficacy of the drug in men with ED of various etiologies, as well as the pos. effect of sildenafil on the quality of a partnership. The most frequent adverse effects documented with sildenafil usage are headache, flushes, dyspepsia, visual disturbances and nasal congestion/rhinitis. These adverse effects are dose-related, usually transient and mild, with low withdrawal rate. Several studies performed recently have shown that sildenafil is a safe and effective treatment of ED in patients with cardiovascular disease, who do not take nitrates or nitrate donors concomitantly. Other oral medications for ED include apomorphine , phentolamine, yohimbine, trazodone, testosterone and new PDE-5 inhibitors in Phase III clin. trials, such as vardenafil and tadalafil. It is obvious, according to recent data, that the concept of PDE-5 inhibition has a central position in oral pharmacotherapy of ED. However, larger clin. studies of efficacy and safety should be carried out using most of the other above-mentioned oral agents and these may also gain a place in the therapy of ED. There are no studies directly comparing sildenafil and other treatments of ED or assessing its role in combination with other therapies. According to the present knowledge, the quality of life, not only of patients but also of their sexual partners, will be improved significantly with sildenafil usage and this is an important precondition for overall health of both. Sildenafil is thus a highly effective peroral treatment for ED in patients without contraindications for its use, which can be considered as the firstline therapy with an acceptable risk-benefit ratio.

ACCESSION NUMBER:

2002:864093 CAPLUS

TITLE:

Erectile dysfunction: oral pharmacotherapy options

AUTHOR(S):

Vitezic, D.; Pelcic, J. Mrsic

CORPORATE SOURCE:

Clinical Pharmacology Unit, University Hospital Center Rijeka and Department of Pharmacology, University of

Rijeka Medical School, Rijeka, Croatia

SOURCE:

International Journal of Clinical Pharmacology and

Therapeutics (2002), 40(9), 393-403

CODEN: ICTHEK; ISSN: 0946-1965 Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal LANGUAGE: English

PUBLISHER:

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

- TI Erectile dysfunction: oral pharmacotherapy options
- Erectile dysfunction (ED) (impotence) is a AΒ widespread, age-related problem, which affects 52% of men between 40 and 70 yr of age. It is classified as psychogenic, org., or mixed psychogenic and org. ED is not a problem only of men, because the relationship between partners can also be disturbed. Therefore, adequate treatment of ED is needed and the most convenient and simplest way is oral drug therapy. Sildenafil, phosphodiesterase-(PDE)-5-selective inhibitor has been the drug of choice for patients with ED since it has been launched in Mar. 1998. The results of various studies have confirmed the efficacy of the drug in men with ED of various etiologies, as well as the pos. effect of sildenafil on the quality of a partnership. The most frequent adverse effects documented with sildenafil usage are headache, flushes, dyspepsia, visual disturbances and nasal congestion/rhinitis. These adverse effects are dose-related, usually transient and mild, with low withdrawal rate. Several studies performed recently have shown that sildenafil is a safe and effective treatment of ED in patients with cardiovascular disease, who do not take nitrates or nitrate donors concomitantly. Other oral medications for ED include apomorphine phentolamine, yohimbine, trazodone, testosterone and new PDE-5 inhibitors in Phase III clin. trials, such as vardenafil and tadalafil. It is obvious, according to recent data, that the concept of PDE-5 inhibition has a central position in oral pharmacotherapy of ED. However, larger clin. studies of efficacy and safety should be carried out using most of the other above-mentioned oral agents and these may also gain a place in the therapy of ED. There are no studies directly comparing sildenafil and other treatments of ED or assessing its role in combination with other therapies. According to the present knowledge, the quality of life, not only of patients but also of their sexual partners, will be improved significantly with sildenafil usage and this is an important precondition for overall health of both. Sildenafil is thus a highly

effective peroral treatment for ED in patients without contraindications for its use, which can be considered as the firstline therapy with an

L1 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2002 ACS

acceptable risk-benefit ratio.

A review. Erectile dysfunction (ED) affects many men and, as the elderly population grows, the incidence of ED and demand for treatment will increase. Many org. and/or psychogenic factors cause or worsen ED. For health-care providers and insurers, the treatment of ED involves direct medical costs (e.g. drug costs and physician visits). Indirectly, the effects of ED on the overall health and mental status of the patient may affect medical and societal costs. Management of ED should include alteration of modifiable risk factors (e.g. lifestyle and psychosocial factors); however, these modifications are frequently insufficient to completely reverse ED. Oral sildenafil 25 to 100 mg is considered first-line direct therapy for ED and is effective in .apprxeq.70% of men with ED. A selective phosphodiesterase type 5 (PDE5) inhibitor, sildenafil improves the ability to attain and maintain erections and increases the rate of successful sexual intercourse in men with ED regardless of their age, presence of other medical conditions and concomitant antihypertensive or antidepressant medications. Sildenafil treatment may be initiated by primary care physicians instead of by

specialists, which decreases costs to healthcare payors. Sildenafil treatment significantly improves quality-of-life related to sexual function and general well being; potential healthcare savings may result as these effects trickle down. Commonly reported adverse events are predominantly transient, mild and dose-related and include headache, flushing, dyspepsia, nasal congestion and abnormal vision. Concurrent administration of sildenafil and org. nitrates is contraindicated because marked hypotension may occur. Sublingual apomorphine (not currently available in the US) and vardenafil and tadalafil (PDE5 inhibitors in late stages of development) are other potential oral treatments for ED. Second-line pharmacol. therapies include intracavernosal injections (alprostadil, papaverine, phentolamine and combinations of these agents) and intraurethral alprostadil. Non-pharmacol. treatments include vacuum constrictor devices and, rarely, vascular surgery or penile implants. In economic models, sildenafil is cost effective compared with no treatment or papaverine/phentolamine injections. The cost-effectiveness of sildenafil compares favorably with that of accepted therapies for other medical conditions. Overall healthcare costs for health plan organizations did not increase significantly with the addn. of sildenafil coverage. Seeking medical attention for ED may contribute to the early detection of serious concomitant conditions and result in long-term redns. in healthcare costs. In conclusion, sildenafil is an effective oral therapy for men with ED of various etiologies. Its efficacy in improving erectile function, ease-of-use and good tolerability profile make sildenafil first-line treatment for men with ED who do not have contraindications to its use.

ACCESSION NUMBER:

CORPORATE SOURCE:

2002:690741 CAPLUS

DOCUMENT NUMBER:

137:226109

TITLE:

Management of erectile dysfunction

: Defining the role of sildenafil

AUTHOR(S):

Lyseng-Williamson, Katherine A.; Wagstaff, Antona J.

Adis International Limited, Auckland, N. Z.

SOURCE:

Disease Management & Health Outcomes (2002), 10(7),

431-452

CODEN: DMHOFV; ISSN: 1173-8790

PUBLISHER:
DOCUMENT TYPE:

Adis International Ltd. Journal; General Review

LANGUAGE:

English

REFERENCE COUNT:

171 THERE ARE 171 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

TI Management of **erectile dysfunction**: Defining the role of sildenafil

A review. Erectile dysfunction (ED) affects many men AΒ and, as the elderly population grows, the incidence of ED and demand for treatment will increase. Many org. and/or psychogenic factors cause or worsen ED. For health-care providers and insurers, the treatment of ED involves direct medical costs (e.g. drug costs and physician visits). Indirectly, the effects of ED on the overall health and mental status of the patient may affect medical and societal costs. Management of ED should include alteration of modifiable risk factors (e.g. lifestyle and psychosocial factors); however, these modifications are frequently insufficient to completely reverse ED. Oral sildenafil 25 to 100 mg is considered first-line direct therapy for ED and is effective in .apprxeq.70% of men with ED. A selective phosphodiesterase type 5 (PDE5) inhibitor, sildenafil improves the ability to attain and maintain erections and increases the rate of successful sexual intercourse in men with ED regardless of their age, presence of other medical conditions and concomitant antihypertensive or antidepressant medications. Sildenafil treatment may be initiated by primary care physicians instead of by

specialists, which decreases costs to healthcare payors. Sildenafil treatment significantly improves quality-of-life related to sexual function and general well being; potential healthcare savings may result as these effects trickle down. Commonly reported adverse events are predominantly transient, mild and dose-related and include headache, flushing, dyspepsia, nasal congestion and abnormal vision. Concurrent administration of sildenafil and org. nitrates is contraindicated because marked hypotension may occur. Sublingual apomorphine (not currently available in the US) and vardenafil and tadalafil (PDE5 inhibitors in late stages of development) are other potential oral treatments for ED. Second-line pharmacol. therapies include intracavernosal injections (alprostadil, papaverine, phentolamine and combinations of these agents) and intraurethral alprostadil. Non-pharmacol. treatments include vacuum constrictor devices and, rarely, vascular surgery or penile implants. In economic models, sildenafil is cost effective compared with no treatment or papaverine/phentolamine injections. The cost-effectiveness of sildenafil compares favorably with that of accepted therapies for other medical conditions. Overall healthcare costs for health plan organizations did not increase significantly with the addn. of sildenafil coverage. Seeking medical attention for ED may contribute to the early detection of serious concomitant conditions and result in long-term redns. in healthcare costs. In conclusion, sildenafil is an effective oral therapy for men with ED of various etiologies. Its efficacy in improving erectile function, ease-of-use and good tolerability profile make sildenafil first-line treatment for men with ED who do not have contraindications to its use. review cavernous smooth muscle relaxant sildenafil erectile dysfunction impotence

ST

IT Sexual behavior

> (impotence; role of sildenafil in management of erectile dysfunction patients)

IT

(role of sildenafil in management of erectile dysfunction patients)

Muscle relaxants IT

(smooth, cavernous; role of sildenafil in management of erectile dysfunction patients)

ΙT 9068-52-4, Phosphodiesterase type 5

> RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; role of sildenafil in management of erectile dysfunction patients)

IT 139755-83-2, Sildenafil

> RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(role of sildenafil in management of erectile dysfunction patients)

L1 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2002 ACS

AB A method for treating sexual dysfunction in a patient taking antidepressant medication in need of such treatment comprises administering a therapeutically effective amt. of apomorphine, or a pharmaceutically acceptable salt thereof. The method may be used for patients taking antidepressants such as tricyclic anti-depressants, monamine oxidase inhibitors, or selective serotonin reuptake inhibitors.

2002:638290 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 137:163826

TITLE: Treatment of antidepressant-induced sexual dysfunction

with apomorphine

INVENTOR(S): Ruff, Dustin D.; Perdok, Renee J.

```
PATENT ASSIGNEE(S):
SOURCE:
                         U.S. Pat. Appl. Publ., 6 pp.
                         CODEN: USXXCO
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                    KIND DATE
                                          APPLICATION NO. DATE
     ----- ---- ---- ----
                                          -----
                            20020822
     US 2002115683 A1
                                         US 2001-993782 20011114
     WO 2002039879
                     A2 20020523
                                          WO 2001-US43933 20011114
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
     US 200235129
                     A5 20020527
                                           US 2002-35129
                                                           20011114
                                        US 2000-249031P P 20001115
PRIORITY APPLN. INFO.:
                                        WO 2001-US43933 W 20011114
     Treatment of antidepressant-induced sexual dysfunction with
TT
     apomorphine
AΒ
     A method for treating sexual dysfunction in a patient taking
     antidepressant medication in need of such treatment comprises
     administering a therapeutically effective amt. of apomorphine,
     or a pharmaceutically acceptable salt thereof. The method may be used for
     patients taking antidepressants such as tricyclic anti-depressants,
     monamine oxidase inhibitors, or selective serotonin reuptake inhibitors.
ST
     antidepressant induced sexual dysfunction treatment apomorphine
IT
     Antidepressants
     Antiemetics
     Human
     Vomiting
        (apomorphine for treatment of antidepressant-induced sexual
        dysfunction)
IT
     Sexual behavior
        (clitoral erectogenesis and vaginal engorgement; apomorphine
        for treatment of antidepressant-induced sexual dysfunction)
IT
    Mental disorder
        (depression; apomorphine for treatment of
        antidepressant-induced sexual dysfunction)
IT
     Sexual behavior
        (disorder; apomorphine for treatment of antidepressant-
        induced sexual dysfunction)
IT
     Sexual behavior
        (impotence; apomorphine for treatment of
        antidepressant-induced sexual dysfunction)
IT
     Drug delivery systems
        (inhalants; apomorphine for treatment of antidepressant-
        induced sexual dysfunction)
IT
    Drug delivery systems
        (nasal; apomorphine for treatment of
       antidepressant-induced sexual dysfunction)
IT
    Drug delivery systems
        (oral; apomorphine for treatment of antidepressant-induced
```

```
sexual dysfunction)
IT
     Biological transport
        (serotonin reuptake inhibitors; apomorphine for treatment of
        antidepressant-induced sexual dysfunction)
ΙT
     Drug delivery systems
        (sublingual; apomorphine for treatment of
        antidepressant-induced sexual dysfunction)
IT
     Antidepressants
        (tricyclic; apomorphine for treatment of antidepressant-
        induced sexual dysfunction)
ΙT
     56296-78-7, Prozac
                          79559-97-0, Zoloft
     RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
     activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (apomorphine for treatment of antidepressant-induced sexual
        dysfunction)
     50-53-3, Chlorpromazine, biological studies
TΤ
                                                   51-34-3, Scopolamine
     54-11-5, Nicotine
                         58-00-4, Apomorphine
                                                58-38-8,
     Prochlorperazine
                        84-04-8, Pipamazine
                                              129-74-8, Buclizine hydrochloride
     134-64-5, Lobeline sulfate 138-56-7, Trimethobenzamide
                                                                303-25-3,
     Cyclizine hydrochloride
                              314-19-2, Apomorphine hydrochloride
     364-62-5, Metoclopramide 523-87-5, Dimenhydrinate
                                                            1420-55-9,
     Thiethylperazine
                       3254-89-5, Diphenidol hydrochloride
                                                             14008-44-7,
     Metopimazine
                    22199-40-2
                                57808-66-9, Domperidone
                                                            99614-02-5,
     Ondansetron
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (apomorphine for treatment of antidepressant-induced sexual
        dysfunction)
IT
     61869-08-7, Paxil
     RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
     activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (clitoral erectogenesis and vaginal engorgement; apomorphine
        for treatment of antidepressant-induced sexual dysfunction)
IT
     9001-66-5, Monoamine oxidase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; apomorphine for treatment of
        antidepressant-induced sexual dysfunction)
IT
     50-67-9, Serotonin, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (reuptake inhibitors; apomorphine for treatment of
        antidepressant-induced sexual dysfunction)
     ANSWER 4 OF 11 CAPLUS COPYRIGHT 2002 ACS
T.1
     A method for treating sexual dysfunction in a patient taking
     antidepressant medication in need of such treatment comprises
     administering a therapeutically effective amt. of apomorphine or
     a pharmaceutically acceptable salt thereof. The method may be used for
     patients taking antidepressants such as tricyclic antidepressants,
     monamine oxidase inhibitors, or serotonin selective reuptake inhibitors.
                         2002:505409 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         137:57597
TITLE:
                         Treatment of antidepressant drug-induced sexual
                         dysfunction with apomorphine
INVENTOR(S):
                         Ruff, Dustin D.; Perdok, Renee J.
PATENT ASSIGNEE(S):
SOURCE:
                         U.S. Pat. Appl. Publ., 6 pp., Cont. of U.S. Ser. No.
                         713,741, abandoned.
                         CODEN: USXXCO
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
```

PATENT NO. KIND DATE APPLICATION NO. DATE ______ -----US 2002086876 **A**1 20020704 US 2001-974136 20011010 PRIORITY APPLN. INFO.: US 2000-713741 B1 20001115 Treatment of antidepressant drug-induced sexual dysfunction with apomorphine AB A method for treating sexual dysfunction in a patient taking antidepressant medication in need of such treatment comprises administering a therapeutically effective amt. of apomorphine or a pharmaceutically acceptable salt thereof. The method may be used for patients taking antidepressants such as tricyclic antidepressants, monamine oxidase inhibitors, or serotonin selective reuptake inhibitors. ST antidepressant sexual dysfunction treatment apomorphine IT Antidepressants Human Vagina (apomorphine for treatment of antidepressant-induced sexual dysfunction) IT Antiemetics (apomorphine for treatment of antidepressant-induced sexual dysfunction, and use with antiemetics) IT Reproductive organ (clitoris; apomorphine for treatment of antidepressantinduced sexual dysfunction) TТ Mental disorder (depression; apomorphine for treatment of antidepressant-induced sexual dysfunction) IT Sexual behavior (disorder; apomorphine for treatment of antidepressantinduced sexual dysfunction) ΙT Toxicity (drug; apomorphine for treatment of antidepressant-induced sexual dysfunction, and use with antiemetics) IT Sexual behavior (impotence; apomorphine for treatment of antidepressant-induced sexual dysfunction) IT Drug delivery systems (inhalants; apomorphine for treatment of antidepressantinduced sexual dysfunction) TΤ Drug delivery systems (nasal; apomorphine for treatment of antidepressant-induced sexual dysfunction) IT Drug delivery systems (oral; apomorphine for treatment of antidepressant-induced sexual dysfunction) IT Drug delivery systems (sublingual; apomorphine for treatment of antidepressant-induced sexual dysfunction) ΙT Antidepressants (tricyclic; apomorphine for treatment of antidepressantinduced sexual dysfunction) IT Biological transport (uptake, selective serotonin reuptake inhibitors; apomorphine for treatment of antidepressant-induced sexual dysfunction) IT 58-00-4, Apomorphine 314-19-2, Apomorphine hydrochloride RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

```
(Biological study); USES (Uses)
        (apomorphine for treatment of antidepressant-induced sexual
        dysfunction)
ייד
     56296-78-7, Prozac 78246-49-8, Paxil 79559-97-0, Zoloft
     RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
     activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (apomorphine for treatment of antidepressant-induced sexual
        dysfunction, and use with antiemetics)
                                                  51-34-3, Scopolamine
     50-53-3, Chlorpromazine, biological studies
IT
     54-11-5, Nicotine
                        58-38-8, Prochlorperazine 84-04-8, Pipamazine
     129-74-8, Buclizine hydrochloride 134-64-5, Lobeline sulfate
     Trimethobenzamide 303-25-3, Cyclizine hydrochloride 364-62-5,
     Metoclopramide
                     523-87-5, Dimenhydrinate
                                                1420-55-9, Thiethylperazine
     3254-89-5, Diphenidol hydrochloride 14008-44-7, Metopimazine 22199-40-2 57808-66-9, Domperidone 99614-02-5, Ondansetron
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (apomorphine for treatment of antidepressant-induced sexual
        dysfunction, and use with antiemetics)
     9001-66-5, Monoamine oxidase
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; apomorphine for treatment of
        antidepressant-induced sexual dysfunction)
IT
     50-67-9, Serotonin, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (selective reuptake inhibitors; apomorphine for treatment of
        antidepressant-induced sexual dysfunction)
     ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS
L1
     Intrasanal delivery compns. and methods for the delivery of dopamine
AB
     receptor agonists are provided which are effective for the treatment of
     sexual dysfunction in a mammal without causing substantial intolerable
     adverse side effects to the mammal, in particular adverse nasal
     effects. Nasally administered compns. for treating sexual
     dysfunction in a mammal are also provided which include a therapeutically
     effective amt. of a dopamine receptor agonist which has been dispersed in
     a system to improve its soly. and/or stability. Examples are provided
     showing that apomorphine-HCl formulated with propylene glycol
     and glycerin did not have the nasal adverse effects assocd. with
     formulations not contg. the glycol. The propylene glycol-
     apomorphine formulation was shown effective in treating patients
     with psychogenic erectile dysfunction.
ACCESSION NUMBER:
                         2002:240569 CAPLUS
DOCUMENT NUMBER:
                         136:252469
TITLE:
                         Nasal delivery of apomorphine in
                         combination with glycol derivatives
INVENTOR(S):
                         Behl, Charajit R.; Romeo, Vincent D.; Achari, Raja G.;
                         Ahmed, Shamin; Demeireles, Jorge C.; Liu, Tianquing;
                         Sileno, Anthony P.
PATENT ASSIGNEE(S):
                         Nastech Pharmaceutical Company, Inc., USA
SOURCE:
                         PCT Int. Appl., 33 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO. KIND DATE
                                         APPLICATION NO. DATE
                                           -----
                            20020328
     WO 2002024202 A1
                                          WO 2001-US29437 20010919
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2001092865
                      A5
                           20020402
                                            AU 2001-92865 20010919
                                         US 2000-665500 A 20000919
PRIORITY APPLN. INFO.:
                                          WO 2001-US29437 W 20010919
REFERENCE COUNT:
                          3
                                THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI
     Nasal delivery of apomorphine in combination with
     glycol derivatives
AB
     Intrasanal delivery compns. and methods for the delivery of dopamine
     receptor agonists are provided which are effective for the treatment of
     sexual dysfunction in a mammal without causing substantial intolerable
     adverse side effects to the mammal, in particular adverse nasal
     effects. Nasally administered compns. for treating sexual
     dysfunction in a mammal are also provided which include a therapeutically
     effective amt. of a dopamine receptor agonist which has been dispersed in
     a system to improve its soly. and/or stability. Examples are provided
     showing that apomorphine-HCl formulated with propylene glycol
     and glycerin did not have the nasal adverse effects assocd. with
     formulations not contg. the glycol. The propylene glycol-
     apomorphine formulation was shown effective in treating patients
     with psychogenic erectile dysfunction.
ST
     apomorphine propylene glycol nasal formulation sexual
     dysfunction
IT
     Sexual behavior
        (disorder; nasal delivery of apomorphine in
        combination with glycol derivs. for treatment of sexual dysfunction)
IT
     Sexual behavior
        (impotence; nasal delivery of apomorphine
        in combination with glycol derivs. for treatment of sexual dysfunction)
IT
     Dopamine agonists
     Human
        (nasal delivery of apomorphine in combination with
        glycol derivs. for treatment of sexual dysfunction)
TΤ
     Glycols, biological studies
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (nasal delivery of apomorphine in combination with
        glycol derivs. for treatment of sexual dysfunction)
IT
     Drug delivery systems
        (nasal; nasal delivery of apomorphine in
        combination with glycol derivs. for treatment of sexual dysfunction)
ΙT
     56-81-5, Glycerin, biological studies 57-55-6, Propylene glycol,
    biological studies
     RL: ADV (Adverse effect, including toxicity); MOA (Modifier or additive
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (nasal delivery of apomorphine in combination with
        glycol derivs. for treatment of sexual dysfunction)
IT
     58-00-4, Apomorphine
                            314-19-2, Apomorphine
    hydrochloride
    RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
     activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (nasal delivery of apomorphine in combination with
```

glycol derivs. for treatment of sexual dysfunction)

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ANSWER 6 OF 11 CAPLUS COPYRIGHT 2002 ACS
L1
     Methods are disclosed for administering apomorphine to a patient
AΒ
      for the treatment of sexual dysfunctions while reducing undesirable side
      effects. In the methods, the concn. of apomorphine is attained
     within the patients' plasma of up to 10 ng per mL. Advantageously, this
      concn. may be achieved with less than 15% of patients so treated
      experiencing emesis. Methods of administration are intranasally
      , by inhalation to the lungs, or by oral ingestion.
ACCESSION NUMBER:
                           2001:747607 CAPLUS
DOCUMENT NUMBER:
                           135:267280
TITLE:
                           Methods for treating sexual dysfunction with
                           apomorphine at specified plasma concentration
                           levels
                           Gupta, Pramod K.; Bollinger, John Daniel; Chen,
INVENTOR(S):
                           Yisheng; Zheng, Jack Yuqun; Reiland, Thomas L.; Lee,
                           Dennis Y.
PATENT ASSIGNEE(S):
                           Tap Holdings, Inc., USA
SOURCE:
                           PCT Int. Appl., 27 pp.
                           CODEN: PIXXD2
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                   KIND DATE
                                       APPLICATION NO. DATE
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                                          WO 2001-US40294 20010314
     WO 2001074358 A1
                              20011011
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
              BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                       Α
     BR 2000005797
                              20011016
                                             BR 2000-5797
                                                               20001208
     CN 1315177
                        Α
                              20011003
                                              CN 2000-137440
                                                                 20001220
     US 2002006933
                        A1
                              20020117
                                              US 2001-808605
                                                                 20010314
PRIORITY APPLN. INFO.:
                                           US 2000-190540P P 20000320
REFERENCE COUNT:
                                 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                           3
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     Methods for treating sexual dysfunction with apomorphine at
TT
     specified plasma concentration levels
     Methods are disclosed for administering apomorphine to a patient
AB
     for the treatment of sexual dysfunctions while reducing undesirable side
     effects. In the methods, the concn. of apomorphine is attained
     within the patients' plasma of up to 10 ng per mL. Advantageously, this
     concn. may be achieved with less than 15% of patients so treated
     experiencing emesis. Methods of administration are intranasally
     , by inhalation to the lungs, or by oral ingestion.
     apopmorphine sexual dysfunction adverse effect redn; nasal
     inhalant oral apomorphine sexual dysfunction; emesis redn
     apopmorphine sexual dysfunction
IT
     Drug bioavailability
     Pharmacokinetics
     Vomiting
```

(apomorphine at specified plasma concn. levels for sexual

dysfunction treatment) IT Drug delivery systems (capsules; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) ITSexual behavior (disorder; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (drops; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Toxicity (drug; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (gels; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) Drug delivery systems IT (granules; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Sexual behavior (impotence; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (inhalants; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Medical goods (inhalers, metered dose and dry powder; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (nasal; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (ointments, creams; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (ointments; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) TT Drug delivery systems (oral; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) TT Drug delivery systems (powders; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (solns., nasal; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (solns.; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (sprays; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (sprinkles and pills; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) ΙT Drug delivery systems (suspensions; apomorphine at specified plasma concn. levels for sexual dysfunction treatment) IT Drug delivery systems (tablets; apomorphine at specified plasma concn. levels for

sexual dysfunction treatment)

IT 58-00-4, Apomorphine

AΒ

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(apomorphine at specified plasma concn. levels for sexual dysfunction treatment)

ANSWER 7 OF 11 CAPLUS COPYRIGHT 2002 ACS L1

A review with 72 refs. Sildenafil is an oral treatment for erectile dysfunction (ED). It acts as an inhibitor of 3',5'-cyclic guanosine monophosphate-phosphodiesterase type 5. An effective treatment for ED is required to produce an erectile response sufficient for satisfactory sexual performance. This has been documented for sildenafil in men with ED of differing etiologies and baseline severity in various types of clin. trials. Sildenafil treatment is characterized by a good tolerability profile and low treatment discontinuation rate caused by treatment-related adverse effects. Most of the adverse effects assocd. with sildenafil are extensions of the pharmacol. action of the drug. There is no significant difference in the adverse effect profile (headache, flushing, dyspepsia, 'nasal congestion and abnormal vision) of this agent as assessed by clin. data obtained either in the pre- and postlaunch periods. Because of its acceptable risk-benefit ratio, sildenafil can be prescribed to a very large group of patients with ED. The reports of serious cardiovascular events assocd. with the use of sildenafil (including anecdotal reports of deaths) have been very thoroughly analyzed. A no. of studies have not shown any difference in the risk of serious cardiovascular events in sildenafil- and placebo-treated patients. However, when making a risk-benefit evaluation, certain subgroups of patients need to be considered sep. In particular, sildenafil is contraindicated in patients receiving nitrate therapy. In some other subgroups of patients, the risks and benefits of treatment need to be assessed on an individual basis and it is hoped that addnl. data will clarify any possible risks assocd. with sildenafil administration such patients. It is helpful to compare the risk-benefit profile of sildenafil with the characteristics of other oral drugs for ED. According to the preliminary data, apomorphine and phentolamine are possible future options for the treatment of ED; however, there needs to be further clin. evaluation of these agents. Initial data have shown that sildenafil can be successfully combined with intracavernosal injection in patients nonresponders to either therapy. conclusion, favorable characteristics make sildenafil suitable for the first-line therapy for a substantial proportion of patients with ED.

ACCESSION NUMBER: 2001:369087 CAPLUS

DOCUMENT NUMBER: 135:235701

TITLE: A risk-benefit assessment of sildenafil in the

treatment of erectile dysfunction

AUTHOR (S): Vitezic, Dinko

CORPORATE SOURCE: Department of Pharmacology, University of Rijeka

> Medical School, Rijeka, Croatia Drug Safety (2001), 24(4), 255-265

CODEN: DRSAEA; ISSN: 0114-5916

PUBLISHER: Adis International Ltd. DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

SOURCE:

REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

A risk-benefit assessment of sildenafil in the treatment of erectile dysfunction

AΒ A review with 72 refs. Sildenafil is an oral treatment for erectile dysfunction (ED). It acts as an inhibitor of 3',5'-cyclic guanosine monophosphate-phosphodiesterase type 5. An effective treatment for ED is required to produce an erectile response sufficient for satisfactory sexual performance. This has been documented for sildenafil in men with ED of differing etiologies and baseline severity in various types of clin. trials. Sildenafil treatment is characterized by a good tolerability profile and low treatment discontinuation rate caused by treatment-related adverse effects. Most of the adverse effects assocd. with sildenafil are extensions of the pharmacol. action of the drug. There is no significant difference in the adverse effect profile (headache, flushing, dyspepsia, nasal congestion and abnormal vision) of this agent as assessed by clin. data obtained either in the pre- and postlaunch periods. Because of its acceptable risk-benefit ratio, sildenafil can be prescribed to a very large group of patients with ED. The reports of serious cardiovascular events assocd. with the use of sildenafil (including anecdotal reports of deaths) have been very thoroughly analyzed. A no. of studies have not shown any difference in the risk of serious cardiovascular events in sildenafil- and placebo-treated patients. However, when making a risk-benefit evaluation, certain subgroups of patients need to be considered sep. In particular, sildenafil is contraindicated in patients receiving nitrate therapy. In some other subgroups of patients, the risks and benefits of treatment need to be assessed on an individual basis and it is hoped that addnl. data will clarify any possible risks assocd. with sildenafil administration such patients. It is helpful to compare the risk-benefit profile of sildenafil with the characteristics of other oral drugs for ED. According to the preliminary data, apomorphine and phentolamine are possible future options for the treatment of ED; however, there needs to be further clin. evaluation of these agents. Initial data have shown that sildenafil can be successfully combined with intracavernosal injection in patients nonresponders to either therapy. In conclusion, favorable characteristics make sildenafil suitable for the first-line therapy for a substantial proportion of patients with ED. review sildenafil interaction cardiovascular system erectile dysfunction

IT Sexual behavior

ST

(impotence; risk-benefit assessment of sildenafil for treatment of erectile dysfunction in humans)

IT Cardiovascular system

Drug interactions

(risk-benefit assessment of sildenafil for treatment of erectile dysfunction in humans)

IT 139755-83-2, Sildenafil

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(risk-benefit assessment of sildenafil for treatment of
erectile dysfunction in humans)

IT 50-60-2, Phentolamine 58-00-4, **Apomorphine** 14797-55-8, Nitrate, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (risk-benefit assessment of sildenafil for treatment of erectile dysfunction in humans)

L1 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2002 ACS

AB Intranasal delivery methods and compns. for the delivery of dopamine receptor agonists are provided which are effective for the amelioration of erectile dysfunction in a mammal without causing substantial intolerable adverse side effects to the mammal. Nasally administered compns. for treating male

erectile dysfunction in a mammal are also provided which include a therapeutically effective amt. of a dopamine receptor agonist which has been dispersed in a system to improve its soly. and/or stability. For example, apomorphine.cntdot.HCl was dispersed in propylene glycol. Its drug soly. was enhanced by 304 % as compared to that of the control system dispersed in water. ACCESSION NUMBER: 2000:900452 CAPLUS DOCUMENT NUMBER: 134:46823

TITLE: Nasal delivery of apomorphine

Achari, Raja G.; Ahmed, Shamim; Behl, Charanjit R.; INVENTOR(S):

Demeireles, Jorge C.; Liu, Tianquing; Romeo, Vincent

D.; Sileno, Anthony P.

PATENT ASSIGNEE(S): Nastech Pharmaceutical Company, Inc., USA

SOURCE:

PCT Int. Appl., 30 pp.

CODEN: PIXXD2

Patent

DOCUMENT TYPE: LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                     KIND DATE
                                                  APPLICATION NO. DATE
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      WO 2000076509
                        A1
                                 20001221
                                                 WO 2000-US4268 20000218
          W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
               CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
               IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
               CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
      US 6436950
                                 20020820
                           B1
                                                  US 1999-334304
                                                                       19990616
      EP 1191933
                           A1
                                 20020403
                                                   EP 2000-914639
                                                                      20000218
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO
     BR 2000012080
                                 20020507
                                                   BR 2000-12080
                         Α
                                                                       20000218
     US 2002161017
                           A1
                                 20021031
                                                   US 2002-62021
                                                                       20020131
     US 2002165249
                           A1
                                 20021107
                                                   US 2002-62020
                                                                       20020131
PRIORITY APPLN. INFO.:
                                               US 1998-96545P
                                                                 P 19980814
                                               US 1999-334304
                                                                   A 19990616
                                               WO 2000-US4268
                                                                   W 20000218
REFERENCE COUNT:
                                     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
```

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TINasal delivery of apomorphine

Intranasal delivery methods and compns. for the delivery of dopamine receptor agonists are provided which are effective for the amelioration of erectile dysfunction in a mammal without causing substantial intolerable adverse side effects to the mammal. Nasally administered compns. for treating male erectile dysfunction in a mammal are also provided which include a therapeutically effective amt. of a dopamine receptor agonist which has been dispersed in a system to improve its soly. and/or stability. For example, apomorphine.cntdot.HCl was dispersed in propylene glycol. Its drug soly. was enhanced by 304 % as compared to that of the control system dispersed in water.

ST nasal delivery dopamine agonist erectile dysfunction; apomorphine propylene glycol soly nasal delivery

IT Paraffin oils

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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (as humectant; nasal delivery of dopamine agonists for
        amelioration of erectile dysfunction)
IT
     Sexual behavior
        (impotence; nasal delivery of dopamine agonists for
        amelioration of erectile dysfunction)
IT
     Dopamine agonists
        (nasal delivery of dopamine agonists for amelioration of
        erectile dysfunction)
IT
     Alditols
     Polyoxyalkylenes, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (nasal delivery of dopamine agonists for amelioration of
        erectile dysfunction)
IT
     Drug delivery systems
        (nasal; nasal delivery of dopamine agonists for
        amelioration of erectile dysfunction)
ΙT
     Fats and Glyceridic oils, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (vegetable, as humectant; nasal delivery of dopamine agonists
        for amelioration of erectile dysfunction)
IT
     50-70-4, Sorbitol, biological studies
                                             56-81-5, Glycerol, biological
     studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (as humectant; nasal delivery of dopamine agonists for
        amelioration of erectile dysfunction)
IT
     9000-01-5, Acacia gum
                           9002-89-5, Polyvinyl alcohol
                                                             9004-32-4,
     Carboxymethyl cellulose
                               9004-64-2, Hydroxypropyl cellulose
                                                                     9004-67-5,
     Methyl cellulose
                        9005-32-7, Alginic acid
                                                 9012-76-4, Chitosan
     11138-66-2, Xanthan gum
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (as thickener; nasal delivery of dopamine agonists for
        amelioration of erectile dysfunction)
IT
     58-00-4, Apomorphine
                            314-19-2, Apomorphine
     hydrochloride
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (nasal delivery of dopamine agonists for amelioration of
        erectile dysfunction)
     50-81-7, L-Ascorbic acid, biological studies 57-55-6, Propylene glycol,
IT
     biological studies
                          134-03-2, Sodium L-ascorbate
                                                         7681-57-4, Sodium
     metabisulfite
                     25322-68-3, Polyethylene glycol
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (nasal delivery of dopamine agonists for amelioration of
        erectile dysfunction)
L1
     ANSWER 9 OF 11 CAPLUS COPYRIGHT 2002 ACS
     The present invention provides a compn. comprising an oil-in-water
AB
     emulsion and a drug dissolved in the emulsion. The oil phase comprises a
     hydroxylated oil, particularly a hydroxylated vegetable oil. The
     preferred hydroxylated vegetable oil is castor oil. An emulsion was
     prepd. contg. flurbiprofen and castor oil.
ACCESSION NUMBER:
                         2000:290810 CAPLUS
DOCUMENT NUMBER:
                         132:313712
TITLE:
                         O/w emulsion comprising an hydroxylated oil
INVENTOR(S):
                         Davis, Stanley Stewart; Illum, Lisbeth
PATENT ASSIGNEE(S):
                         West Pharmaceutical Services Drug Delivery & Clinical
                         Research Centre, L, UK
SOURCE:
```

PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT ASSIGNEE(S):

DOCUMENT TYPE:

SOURCE:

LANGUAGE:

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PATENT NO.
                      KIND DATE
                                             APPLICATION NO. DATE
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          000024373 A1 <u>20000504</u> WO 1999-GB3489 19991021
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
     WO 2000024373
              CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
              SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,
              BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
              DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
              CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9963536
                                            AU 1999-63536
                        A1 20000515
     EP 1123085
                              20010816
                        A1
                                             EP 1999-950947
                                                              19991021
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO
     NO 2001001985
                              20010423
                                                                20010423
                        Α
                                              NO 2001-1985
     US 2001055569
                        A1
                              20011227
                                             US 2001-841228
                                                                20010424
                                                          A 19981024
PRIORITY APPLN. INFO.:
                                           GB 1998-23246
                                                             W 19<del>991</del>021
                                           WO 1999-GB3489
REFERENCE COUNT:
                           3
                                 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT
     Sexual behavior
         (impotence; oil-water emulsion comprising an hydroxylated
        oil)
IT
     Drug delivery systems
         (nasal; oil-water emulsion comprising an hydroxylated oil)
TT
     53-86-1, Indomethacin
                             58-00-4, Apomorphine
                                                      22204-53-1,
     Naproxen
     RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
         (oil-water emulsion comprising an hydroxylated oil)
L1
     ANSWER 10 OF 11 CAPLUS COPYRIGHT 2002 ACS
     This invention provides a method of rapidly and reliably delivering
AΒ
     sildenafil or derivs. thereof, alone or in combination with other compds.,
     to the systemic circulation by administration via the nasal
     route so as to produce virtually instantaneous onset of beneficial effects
     in the treatment of erectile dysfunction. The present
     invention further provides pharmaceutical compns. comprising sildenafil or
     derivs. thereof, and/or pharmaceutically acceptable salts thereof in a
     variety of unique pharmaceutical dosage forms, with and without
     apomorphine.
ACCESSION NUMBER:
                          1999:819248 CAPLUS
DOCUMENT NUMBER:
                          132:54900
TITLE:
                          Nasal administration of sildenafil for the
                          treatment of erectile dysfunction
INVENTOR(S):
                          Hussain, Anwar A.; Dittert, Lewis W.; Traboulsi,
                          Ashraf
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Delacroix

PCT Int. Appl., 29 pp.

CODEN: PIXXD2

Patent

English

New Millennium Pharmaceutical Research, Inc., USA

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PATENT NO.
                     KIND DATE
                                            APPLICATION NO. DATE
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                                             ------
                              19991229
     WO 9966933
                       A1
                                            WO 1999-US14378 19990624
         W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
              RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
              ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
              CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 6200591
                       B1
                            20010313
                                             US 1998-208439
                                                                19981210
     AU 9945838
                        A1
                              20000110
                                             AU 1999-45838
                                                                19990624
PRIORITY APPLN. INFO.:
                                          US 1998-90740P P 19980625
                                          US 1998-208439
                                                           A 19981210
                                          WO 1999-US14378 W 19990624
REFERENCE COUNT:
                          9
                                 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
ΤI
     Nasal administration of sildenafil for the treatment of
     erectile dysfunction
AB
     This invention provides a method of rapidly and reliably delivering
     sildenafil or derivs. thereof, alone or in combination with other compds.,
     to the systemic circulation by administration via the nasal
     route so as to produce virtually instantaneous onset of beneficial effects
     in the treatment of erectile dysfunction. The present
     invention further provides pharmaceutical compns. comprising sildenafil or
     derivs. thereof, and/or pharmaceutically acceptable salts thereof in a
     variety of unique pharmaceutical dosage forms, with and without
     apomorphine.
ST
     nasal pharmaceutical sildenafil erectile
     dysfunction
IT
     Sexual behavior
         (impotence; nasal administration of sildenafil and
        vasoactive drugs for treatment of erectile
        dysfunction)
IT
     Vasoconstrictors
        (nasal administration of sildenafil and vasoactive drugs for
        treatment of erectile dysfunction)
     Drug delivery systems
IT
        (nasal sprays; nasal administration of sildenafil
        and vasoactive drugs for treatment of erectile
        dysfunction)
IT
     Drug delivery systems
        (nasal, gels; nasal administration of sildenafil
        and vasoactive drugs for treatment of erectile
        dysfunction)
IT
     314-19-2, Apomorphine hydrochloride
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (nasal administration of sildenafil and apomorphine
        for treatment of erectile dysfunction)
     50-60-2, Phentolamine 58-74-2, Papaverine
TT
                                                      59-96-1, Phenoxybenzamine
     139755-83-2, Sildenafil
                               171599-83-0, Sildenafil citrate 252920-86-8
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
```

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(nasal administration of sildenafil and vasoactive drugs for treatment of erectile dysfunction)

ANSWER 11 OF 11 CAPLUS COPYRIGHT 2002 ACS T.1

A compn. for the nasal delivery of a drug suitable for the AB treatment of erectile dysfunction to a mammal is adapted to provide an initial rise in plasma level followed by a sustained plasma level of the drug. Examples given were apomorphine in a pectin based formulation and a Pluronic F127 formulation.

ACCESSION NUMBER:

1999:372055 CAPLUS

DOCUMENT NUMBER:

131:23522

TITLE:

Compositions for nasal administration

INVENTOR(S):

Illum, Lisbeth; Watts, Peter James

PATENT ASSIGNEE(S):

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	9927 W:	905 AL, DK, KG, MX,	AM, EE, KP, NO, UA,	AT, ES, KR, NZ, UG,	AU, FI, KZ, PL, US,		BA, GD, LK, RO, VN,	BB, GE, LR, RU, YU,	BG GH LS SD ZW	NO 1: , BR , GM , LT , SE	998-G , BY, , HR, , LU, , SG,	B357 CA, HU, LV, SI, BY,	CH, ID, MD, SK, KG,	1998; CN, IL, MG, SL, KZ,	 1127 CU, IS, MK, TJ, MD,	CZ, JP, MN, TM,	KE, MW, TR, TJ,	TM	
		FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC	, NL	, PT,								
CA	2312		•			ML, 1999						3128	39	1998:	1127				
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	1035																		
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REFERENCE COUNT:					4	TI Ri		ARE	4 (CITE		EREN	CES	AVAI	LABL				

TT Compositions for nasal administration

AΒ A compn. for the nasal delivery of a drug suitable for the treatment of erectile dysfunction to a mammal is adapted to provide an initial rise in plasma level followed by a sustained plasma level of the drug. Examples given were apomorphine in a pectin based formulation and a Pluronic F127 formulation.

ST nasal apomorphine formulation; erectile dysfunction apomorphine nasal

Dopamine antagonists

(D2; nasal formulations for erectile dysfunction)

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IT
     Sexual behavior
        (impotence; nasal formulations for erectile
        dysfunction)
ΙT
     Drug delivery systems
        (microspheres; nasal formulations for erectile
        dysfunction)
     Drug bioavailability
ΙT
        (nasal formulations for erectile
        dysfunction)
     Polysaccharides, biological studies
IT
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (nasal formulations for erectile
        dysfunction)
IT
     Drug delivery systems
        (nasal; nasal formulations for erectile
        dysfunction)
IT
     Adrenoceptor antagonists
        (.alpha.-; nasal formulations for erectile
        dysfunction)
IT
     58-00-4, Apomorphine
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PEP (Physical, engineering
     or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC
     (Process); USES (Uses)
        (nasal formulations for erectile
        dysfunction)
IT
     9000-69-5, Pectin
                         9004-32-4, Carboxymethyl cellulose
                                                              9004-61-9,
     Hyaluronic acid 9005-32-7, Alginic acid 9012-76-4, Chitosan
     9057-06-1, Carboxymethyl starch 11138-66-2, Xanthan
                                                             71010-52-1, Gellan
     88306-53-0, 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with
     .alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl)
                                                             106392-12-5,
     Pluronic F127
                     110617-70-4, Poloxamine
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (nasal formulations for erectile
        dysfunction)
IT
     50-60-2, Phentolamine 54-32-0, Moxisylyte
                                                   58-74-2
                                                             59-96-1,
     Phenoxybenzamine 74-79-3, L-Arginine, biological studies 146-48-5,
     Yohimbine
                 19794-93-5, Trazodone 38212-33-8, 1-(4-
     Chlorophenyl) piperazine
                              119905-05-4, Delequamine
                                                         139755-83-2
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (nasal formulations for erectile
        dysfunction)
IT
     50-67-9, Serotonin, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (reuptake inhibitors; nasal formulations for erectile
        dysfunction)
     9068-52-4, Cyclic-GMP phosphodiesterase
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (type V, inhibitors; nasal formulations for erectile
        dysfunction)
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Delacroix

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